REMARKS

This responds to the Office Action mailed on November 25, 2009.

Claim 1 is amended and claims 9-10 are added. Claims 1-7 and 9-10 are pending.

Claims 1-7 were rejected under 35 U.S.C. § 103(a) as being obvious over Kreutzer et al. (U.S. Publication No. 2004/0001811), Elbashir et al. (Methods, 26:199 (2002)), Nilsen et al. (U.S. Patent No. 6,013,447), De Young et al. (Biochemistry, 33:12127 1994)), Hernandez (EMBO, 4:1827 (1985)), and Skuzeski et al. (J. Biol. Chem., 259: 8345 (1984)). This rejection, as it may be maintained with respect to the pending claims, is respectfully traversed.

Kreutzer et al. disclose a double stranded (ds) RNA with a RNA strand having a region that is less than 25 nucleotides in length and complementary to at least a portion of a RNA transcript of an anti-apoptotic gene such as Bcl-2. Kreutzer et al. also disclose that the individual strands of a dsRNA can be expressed from two separate vectors or from the same vector, or as an inverted repeat joined by a linker polynucleotide so as to form a stem and loop structure, and that the promoter can be a PolI promoter, PolII promoter, PolIII promoter or a prokaryotic promoter. However, the ssRNAs used to prepare dsRNAs for transfection in the Examples were prepared by conventional oligonucleotide chemical syntheses.

The dsRNAs in the Example in Kreutzer et al. have the following ends:

5′-**CAGG**————————**GACC**-3'

3′-CG**GUCC**————————**CUGG**-5'

5′-**GCC**————————**GCC**-3'

3′-UA**CGG**————————**CGG**-5' and

5′-CA**AGG**————————**GC**A-3'

3′-UCUG**UCC**————————**CG**-5'.

Elbashir et al. disclose the use of small interfering RNAs (siRNAs; 21 to 23 nucleotides in length), which are the products of RNase III digestion of dsRNAs formed with mRNA, to silence genes in mammalian cells. It is disclosed that the predominant siRNAs formed in cells

are 21 and 22 nucleotide RNAs with symmetric 2 nucleotide 3′ overhangs (see Figure 4B which shows "TT" overhangs). Elbashir et al. disclose that 21 nucleotide RNAs useful to form siRNAs are prepared via conventional oligonucleotide chemical syntheses and annealed prior to transfection.

Thus, neither Kreutzer et al. nor Elbashir et al. provide vectors for expressing siRNAs. Moreover, the products disclosed in Kreutzer et al. and Elbashir et al. have two 5' ends and two 3' ends in contrast to the products produced by Applicant's vectors. Further, the sequence in the 3' overhang in the products disclosed in Kreutzer et al. and Elbashir et al. is different than the 3' overhang in the products produced by Applicant's vectors.

Nilsen et al. relate to vectors and methods to identify affector RNA molecules that inhibit expression of target RNA molecules (abstract).

De Young et al. disclose the use of vectors with a U1 snRNA promoter and U1 snRNA terminator sequence, and a T7 promoter and T7 terminator sequence, to express ribozymes.

Hernandez discloses a vector to detect the processing of U1 nuclear RNA, which is transcribed by PolII and is involved in mRNA splicing. The vector includes an internally deleted U1 gene expressed from the SV40 promoter/enhancer. The vector was introduced to cells and the resulting RNA analyzed. The results showed that the first U1 RNA precursor has a few extra nucleotides at the 3′ end which are shortened to form mature U1 RNA, and that a 13 nucleotide sequence 3′ of the coding region is required to direct the first step in the formation of the 3' end of U1 snRNA.

Skuzeski et al. disclose the identification of two regions at the promoter essential for transcription of human U1 RNA and that there is a *Bgl*II site immediately 5′ to the U1 coding region (Figure 5).

The Examiner asserts that the use of any one particular promoter would be a design choice by one of ordinary skill in the art and, given that De Young et al. teach the advantages of using an expression vector system with a U1 promoter for expression of inhibitory molecules such as ribozymes, it would have been obvious to use this vector for expression of dsRNA.

Applicant respectfully disagrees. Although Nilsen et al., DeYoung et al., Hernandez, and Skuzeki et al. disclose expression vectors, some of which include a U1 snRNA promoter or a U1 snRNA terminator sequence, none of those vectors express a siRNA or miRNA.

And as the documents relating to siRNA (Kreutzer et al. and Elbashir et al.) employ conventional oligonucleotide chemical syntheses to prepare individual ssRNAs, and the U1 based vectors in Hernandez and Skuzeski et al. were employed to detect *cis*-acting elements in the U1 gene, the combination of the cited documents does not provide a reasonable expectation that any particular vector, much less Applicant's vectors, could be employed to provide for correct, stable and effective expression in mammalian cells of a siRNA or a miRNA.

In this regard, the Examiner is requested to consider that the product of the vectors of De Young et al. (the document the Examiner specifically relies on in support of the rejection on page 4 of the Office Action) is an enzyme which, in contrast to the product of Applicant's vectors, has catalytic activity and so need not be expressed at particularly high levels to be effective.

Moreover, none of the cited documents individually or in combination with each other disclose or suggest an expression vector that encodes a siRNA or miRNA product with additional nucleotide(s) at the 3' end and optionally 5' end (see, for instance, claim1 as amended, and claims 3-4 and 10), and that allows for siRNA strand selection into the interference complex (see claim 9). Expression from the latter vector can decrease the accumulation of the sense strand into complexes which could mediate undesired targeting. As shown in Figure 3B, a vector of the invention provides transcripts that have specificity and allow for significant interference.

Accordingly, withdrawal of the § 103 rejection is respectfully requested.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's representative at (612) 373-6959 to facilitate prosecution of this application.

If necessary, please charge any additional fees or deficiencies, or credit any overpayments to Deposit Account No. 19-0743.

Respectfully submitted,

SCHWEGMAN, LUNDBERG & WOESSNER, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6959

Date January 25, 2010 By /Janet E. Embretson/
Janet E. Embretson
Reg. No. 39,665

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 25th day of January, 2010.

CHERYL L. KNAPP /Cheryl L Knapp/
Name Signature